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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/036,869	11/29/2001	A. James Mixson	38147-0017	9568

26633 7590 08/09/2005

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/036,869	MIXSON, A. JAMES	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-35 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-35 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 November 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/10/05 has been entered.

Claims 21-35 and 41 are pending and under consideration in this Office Action.

Priority

This case is a continuation of 09/500,838, which is a continuation in part of 08/985,526, now abandoned, which is a continuation in part of 08/680,845, filed 12/5/97, now issued as US Patent 6,080,728. Instant claims 21-35 and 41 are drawn to methods of inhibiting tumor growth through administration of a nucleotide sequence in a in a carrier that is either liposomes, cationic polymers, micelles. The claim term "nucleotide sequence" is interpreted by the Examiner to include RNAs in view of the specification as filed at page 19, lines 4-6 which states "[i]n a further embodiment, RNA carries the coding sequence of antiangiogenic genes." As such, the claims continue to embrace methods of inhibiting tumor growth through administration of RNA. As noted previously, neither 08/985,526 nor the '728 patent provides support for the use of RNA in the invention because these documents are wholly focused on the delivery of DNA and do not in any way contemplate the use of RNA. Because the claims embrace

methods of delivering RNA, their priority date is considered to be 2/10/00, the filing date of 09/500,838.

Response to Arguments

Applicant's arguments filed 6/10/05 have been fully considered but they are not persuasive. The issue of priority is addressed at pages 4-7 of the response. In the following discussion the phrases "parent applications" and "priority documents" refer to the 08/985,526 application and the 08/680,845 application (the '728 patent), and not to the 09/500,838 application.

Applicant's argument is based on the position that support for RNA embodiments of the instant claims can be found in the parent applications in the term "nucleotide". Applicant argues at page 4 that the term "nucleotide" is a common term and well understood term in the biological sciences and is known to include both DNA and RNA. The Examiner agrees, the term "nucleotide" can be used to refer to RNA, to DNA, or to both if used in a generic sense. However, the term "nucleotide" is not used in a generic sense in the parent applications. Instead, the term nucleotide is used only to describe DNA molecules. To demonstrate this, each of the four instances of the term "nucleotide" in the '728 patent is reproduced below with "nucleotide(s)" in emphasis.

Column 7: lines 40-44:
(i) a fragment of thrombospondin I (TSPf) having the amino acid sequence shown in SEQUENCE ID NO: 1. This fragment is encoded by the DNA sequence (nucleotides 1013-1650 of the TSPI gene) shown in SEQUENCE ID NO: 2.

Paragraph bridging columns 8 and 9:
The heterogeneous concatamers need not be limited to only anti-angiogenic peptides. For example, the protein angiostatin or the large polypeptide fragment of prolactin can be modified with genes encoding anti-angiogenic peptides. Again, the concatameric number will vary depending on the number of nucleotide bases of the unit angiogenic inhibitor. In a concatamer of large and small anti-angiogenic

inhibitors, the ratio of large to small inhibitors is 0.1 to 0.9, preferably 1:1.

Column 10, lines 53-56:
TSPf vector is a vector containing a DNA fragment of the TSPI gene which has the two anti-angiogenic domains (nucleotides 992-1650) (Tolsma et al, supra), and a start codon and a stop codon.

Column 10, lines 57-67:
The DNA fragment was prepared by PCR using thrombospondin I cDNA as template, and 100 pmoles of each of the following primers 5'-TAGGTCTAGAATGACTGAAGAGAACAAAGAG-3' (SEQUENCE ID NO: 32) and 5'-ATGGTCTAGATTAGAGACGACTACGTTTCTG-3' (SEQUENCE ID NO: 33) to amplify nucleotides 1013 to 1650 of the TSPI gene. Both primers contain XbaI sites (underlined), the first primer contains an ATG start codon (in bold), and the second primer contains a TTA stop codon (reverse orientation in bold).

It is clear that column 7, lines 40-44, and column 10, lines 53-56 refer to nucleotides in the context of DNA because the first passage refers to a DNA sequence, and the second passage refers to a DNA fragment. It is clear that the PCR primers at column 10, lines 57-67 are DNA because they contain thymidine residues and not uracil residues. There is no reason to expect that they are chimeric molecules of RNA and DNA residues because this is not disclosed in the specification, nor is it routine in the art to perform PCR with such chimeric primers.

Finally, as discussed in detail in the previous Action, the paragraph bridging columns 8 and 9 refers to DNA and not to RNA. This is apparent when the passage is examined in the appropriate context, i.e. the specification from column 7, line 37 through the passage in question. Column 7, lines 37-39 state: "The particular anti-angiogenic protein or peptide encoded by the anti-angiogenic DNA is not critical to the present invention. Examples of suitable peptides include:". This passage is followed by a list of 16 DNA sequences from column 7, line 40 to column 8, line 33. The next paragraphs at column 8, lines 34-56 indicate that the invention is not limited to these

precise DNA sequences, noting that the DNA sequences can be used in concatemeric form. Column 8, line 57-65 to column 9, line 7 are reproduced below.

> Since more than one anti-angiogenic pathway exists, concatamers consisting of two or more types of inhibitor could be more effective than homogenous concatamers. For example, heterogeneous concatamers of TSPI and the fibronectin inhibitors can be inserted into the same vector. An example of such a heterogenous concatamer encoding DNA is shown in SEQUENCE ID NO: 31. In such heterogenous concatamers, the peptide-encoding repeats of each sequence may be linked in blocks and/or randomly.
>
> The heterogeneous concatamers need not be limited to only anti-angiogenic peptides. For example, the protein angiostatin or the large polypeptide fragment of prolactin can be modified with genes encoding anti-angiogenic peptides. Again, the concatameric number will vary depending on the number of **nucleotide** bases of the unit angiogenic inhibitor. In a concatamer of large and small anti-angiogenic inhibitors, the ratio of large to small inhibitors is 0.1 to 0.9, preferably 1:1.

The instance of the term "nucleotide" relied upon by Applicant to support the disclosure of RNA is shown above in bold. In the specification of '728, this term is used to describe the length of a concatemeric sequence encoding one or more angiogenesis inhibitors. It is clear from the '728 specification as a whole, particularly from column 7, line 37 to column 9, line 7, that the term "nucleotide" at column 9, line 4 was used to describe a DNA nucleotide, because this passage of the specification is directed to a discussion of DNAs, not RNAs or nucleic acids broadly. As such, it is clear that the plain meaning of the term "nucleotide", as used in the parent applications, was "DNA nucleotide." There is no support for broadening the interpretation of "nucleotide" in the parent applications to include RNA. It is consistently and specifically used in the parent applications in the context of DNA and not RNA. In contrast, it is clear that the term "nucleotide" in the instant specification embraces RNA. See the instant specification at page 19, lines 4-6. So, the claims continue to embrace RNA, and to the extent that they do, they lack support in the '526 parent application and the '728 patent.

At page 5, first and second paragraphs, Applicant submits that the Examiner has reasoned that the generic term "nucleotide" that includes both RNA and DNA is not supported because the parent application does not provide examples of RNA." This is an inaccurate representation of the Examiner's reasoning. As discussed above, the Examiner agrees that when used in a generic fashion the term "nucleotide" would include RNA and DNA nucleotides. However, the parent applications do not use the term "nucleotide" in a generic fashion. The parent applications use the term "nucleotide" only in reference to DNA nucleotides for the reasons set forth in detail above. As a result, Applicants argument at page 5, first paragraph that "the Examiner has not provided evidence or reasoning for why a lack of RNA examples means that the term "nucleotide" lacks adequate written description" is not on point and ignores the fact that the priority documents use the term "nucleotide" only in the context of describing DNA molecules. Further, Applicant's submission that "the sole basis for the Examiner's rejection is that the claimed recitation of a "nucleotide" genus is not adequately supported because the Patent Application fails to contain RNA samples" is incorrect. As discussed above, the parent applications lack any recitation or representation of the term "nucleotide" as a genus term. Instead, the term is used solely in describing DNA molecules. As a result, Applicant's arguments at page 6, first and second paragraphs, based on the term "nucleotide" as a genus term embracing RNA are unpersuasive.

Applicant asserts at page 6, third full paragraph that the Examiner has provided no evidence for why one skilled in the art would fail to recognize that RNA nucleotides

would be operable in the claimed invention. The issue at hand is not whether or not one of skill would recognize the functionality of RNA in the claimed invention. The issue at hand is whether or not the priority documents support the use of RNA in the claimed invention. The fact that an invention may be obvious or enabled in view of the prior art does not necessarily mean that the invention was adequately described, or disclosed at all, by the original specification. Applicants are reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C 112 is severable from its enablement provision (see *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, page 1115). In this case, the priority documents do not disclose or contemplate in any way the use of RNA in the invention. Even if one of ordinary skill in the art would immediately recognize that RNA could be used in place of DNA, that does not mean that the priority documents described or disclosed the use of RNA. In fact, they do not.

Applicant argues at page 7 that the term "nucleotide" should be given its ordinary and customary meaning as attributed by those of skill in the art, and that this should support RNA. This is unpersuasive. If one reviews the specification of each priority document as a whole, one cannot find any support whatsoever for the use of RNA in the invention. Support for RNA cannot be extracted from the term "nucleotide" when that term is used in the priority documents solely in describing DNA molecules. When the term "nucleotide" is used in the description of DNA molecules, one of skill in the art would understand it to mean "DNA nucleotides", not "RNA and DNA nucleotides". For these reasons the priority date of the instant claims is 2/10/00, the filing date of 09/500,838.

It should also be noted that even if Applicant was able to establish that the priority applications supported RNAs encoding anti-angiogenic peptides and proteins, the instant claims would still not be entitled to the claimed priority date. This is because the neither the priority applications nor the instant application as filed supports methods of inhibiting tumor angiogenesis by inhibiting expression of angiogenic proteins and peptides by use of antisense, ribozymes, siRNA or transcriptional inhibitors, even though the claims as amended embrace these methods. This is discussed more fully under the new matter rejection below.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321□ may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21-35 and 41 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 16, and 17

of U.S. Patent No. 6,080,728 ('728). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Instant claims 21-25, 32, 33, and 41 are methods of inhibiting tumor growth in a subject bearing a tumor by administering in a carrier a nucleic acid that inhibits tumor angiogenesis, wherein the carrier is selected from the group consisting of liposomes, cationic polymers, micelles, and a combination thereof. Instant claims 26-31, 34, and 35 are more broadly drawn to methods of providing anti-angiogenic therapy using the same method steps as those in claims 21-25, 32, 33, or 41. Instant claims 22 and 37 require intravenous injection. Instant claims 23-25 and 29-31 limit the nature of the carrier to species recited in independent claims 21 and 26.

Claim 1 of '728 is drawn to a method of inhibiting tumor growth by administering to a subject a DNA encoding an anti-angiogenic protein with a carrier which may be a liposome, a micelle, or a cationic polymer. Claim 2 requires intravenous injection, and claims 3-5 require a liposomal carrier, a cationic polymer carrier, or a micelle carrier, respectively. These claims anticipate, and render obvious, instant claims 21-27 and 29-31.

Instant claims 28 and 41, require injection into a tumor. These claims are obvious because claim 1 of '728 is broadly drawn to "inhibiting tumor growth by administering to a subject a DNA encoding an anti-angiogenic protein", and clearly embraces intratumoral injection. One of ordinary skill in the art wishing to understand the intended breadth of the claim term "administering" would refer to the specification, e.g. at detailed description paragraph 46 which states:

The particular mode of administering the carrier:DNA complex of the present invention depends on various factors, but preferred modes include intravenous, subcutaneous or **intratumoral injection**. Intravenous injection is the preferred administration mode for distribution of the complex to the developing blood vessels of the tumor.

Emphasis added. Thus claim 1 clearly embraces intratumoral injection.

Instant claims 32-35 require administering a nucleic acid encoding a tumor suppressor such as p53. These claims are obvious over claims 16 and 17of '728, which require "injection of DNA encoding at least one anti-angiogenic protein or peptide and DNA encoding a tumor suppressor protein". Claim 17 requires that the tumor suppressor protein is p53

At page 7 of the response, Applicant requests that the rejection be held in abeyance until the claims are in condition for allowance, "as is permitted in the M.P.E.P." The Examiner is unaware of any provision for holding a rejection in abeyance, and Applicant has failed to point to any. The rejection is not held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 21-35 and 41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 21-35 and 41 are drawn to the genus of nucleotide sequences that inhibit tumor angiogenesis. The specification supports nucleotide sequences encoding at least one anti angiogenic protein or peptide. The specification provides no written support for the broader genus of nucleotide sequences that inhibit tumor angiogenesis. This genus would include nucleic acids encoding antisense and ribozyme molecules that inhibit the expression of angiogenesis stimulating proteins and peptides, small interfering RNAs, as well as nucleic acids that encode transcriptional repressors of angiogenic genes. The specification fails to describe a single example of such a nucleic acid. This disclosure is not sufficient to convey to one of skill in the art that Applicant was in possession of the claimed genus at the time of the invention. The claims should be limited to nucleotide sequences encoding at least one anti angiogenic protein or peptide.

Response to Arguments

Applicant's arguments filed 6/10/05 have been fully considered but they are not persuasive. The issue of new matter is addressed at pages 7 and 8 of the response.

Applicant argues that when one of skill in the art would recognize that the enumerated species in the specification would be clearly operable for other species in a genus claim, then the mention of even a single species provides adequate written description. Applicant submits that the disclosed DNA embodiments provide support for ribozymes, antisense, small interfering RNAs, and nucleic acids that encode

transcriptional repressors of angiogenic genes, given the level of skill in the art and the Examiner's finding that DNA and RNA are recognized equivalents for the purpose of expressing proteins.

This is unpersuasive. The written description requirement can be satisfied by disclosure of a representative number of species or the description of relevant identifying characteristics such as a known or disclosed correlation between structure and function. In this case, the only nucleotide sequences that inhibit angiogenesis that are disclosed in the specification are nucleotide sequences that encode peptides and proteins that directly inhibit angiogenesis such as are listed at page 6, lines 1-14. The specification does not disclose a single example of any ribozyme, antisense RNA, or siRNA, or any nucleic acids that encode transcriptional repressors of angiogenic genes. These RNAs and proteins inhibit angiogenesis through mechanisms that are distinct from those of the proteins listed at page 6. As such, description of peptide and polypeptide angiogenesis inhibitors could not possibly serve as an adequate description of the rest of the claimed genus.

Applicant submits that support for the use of RNA antisense, ribozymes, or transcriptional repressors is inherent in the specification because it would necessarily be understood by the skilled artisan that the use of RNA as a nucleotide according to the specification would be accompanied by the use of RNA that would correspond to an angiogenic protein or peptide. This submission is unpersuasive because it is only a statement of opinion and lacks evidentiary or logical support. Applicant failed to point to a single angiogenic protein or peptide disclosed in the specification that could be

targeted for inhibition by antisense, ribozyme, or transcriptional inhibitor. Applicant also failed to explain why disclosure of antiangiogenic proteins and peptides amounts to an inherent disclosure of antisense and ribozymes directed against mRNAs of angiogenic peptides and proteins. Obviously the function of anti-angiogenic proteins is opposite of that of angiogenic proteins, and Applicant did not give any reason why there would be any structural relationship between these proteins of opposite functional characteristics that would support the idea that disclosure of one class amounts to an inherent disclosure of antisense and ribozyme agents directed against the other class. For these reasons the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21-35 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Mixson (EP 0 819 758 A2, published 1/21/98).

Mixson teaches methods of inhibiting tumor growth in a subject bearing a tumor, which comprises intravenous or intratumoral injection of DNA encoding an anti-angiogenic peptide provided with a carrier selected from the group consisting of cationic lipids, liposomes, and cationic polymer carriers. Mixson also coadministers an

expression vector for p53. See e.g. page 5, lines 24-26 and 33-38; page 15, lines 41-43; and page 17, lines 2-46.

Thus Mixson anticipates the claims.

The PTO recognizes that Applicant has a chain of support for DNA embodiments that includes Mixson (1998). This rejection is considered valid because the rejected claims have been assigned a priority date of 2/10/00, due to the fact that they are drawn to "nucleic acids" and therefore embrace matter not disclosed in the priority documents, e.g. RNA.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21-24, 26-31, 33-35, and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mixson (EP 0 819 758 A2, published 1/21/98) in view of Lu et al (Cancer Gene Therapy, 1(4): 245-252).

Mixson teaches methods of inhibiting tumor growth in a subject bearing a tumor, which comprises intravenous or intratumoral injection of DNA encoding an anti-angiogenic peptide provided with a carrier selected from the group consisting of cationic lipids, liposomes, and cationic polymer carriers. Mixson also coadministers an

expression vector for p53. See e.g. page 5, lines 24-26 and 33-38; page 15, lines 41-43; and page 17, lines 2-46.

Mixson does not teach the use of RNA.

Lu teaches direct delivery to tumors in vivo of liposome/mRNA complexes, stating that liposome/DNA expression vector complexes and liposome/mRNA complexes gave comparable transfection efficacy. See also Fig. 7 on page 251 which shows an approximate 2 fold difference in expression between DNA and RNA transfection in vivo.

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute mRNA for DNA in the method of Mixson. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). Furthermore, MPEP 2144.07 indicates that the selection of a known material based on its suitability for its intended use supports the determination of prima facie obviousness. See also Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945). In this case, mRNA is recognized in the art as having comparable efficacy to DNA for in vivo delivery and expression, so it would have been obvious to substitute one for the other.

Thus the invention as a whole was prima facie obvious.

Claims 25 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mixson (EP 0 819 758 A2, published 1/21/98) and Lu et al (Cancer Gene Therapy, 1(4): 245-252), as applied to claims 21-24, 26-31, 33-35, and 41 above, and further in view of Lee et al (US Patent 5,908,777, issued 6/1/99).

The teachings of Mixson and Lu are detailed above. These references do not explicitly teach a micelle carrier

Lee teaches that micelles are art-recognized equivalents of liposomes and cationic polymers. See Detailed Description paragraph 12 which states:

"The category of suitable cationic helper molecules is illustrated by (1) non-monovalent cations such as Ca.sup.2+, Mg.sup.2+, Mn.sup.2+, Al.sup.3+, and spermidine, (2) cationic polymers such as polylysine, DEAE-dextran, spermine, spermidine, protamine, polybrene, cationized proteins, cationic micelles and cationic liposomes, and (3) cationic detergents such as DC-chol, cetyltrimethylammonium bromide (CTAB), etc."

As stated above MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious.

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 6/10/05 have been fully considered but they are not persuasive. The obviousness rejections are addressed at page 9 of the response. Applicant argues essentially that the rejections are based on the assumption that the instant claims are not adequately supported by the priority documents, and that this

assumption is invalid for the reasons set forth at pages 4-7 of the response, such that the Mixon reference is not available as prior art. These arguments were addressed above, and were found to be unpersuasive, so the rejections are maintained.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Richard Schnizer, Ph.D.